

Mechanical load on the ventilatory muscles during an incremental cycle ergometer test

T. Wanke, D. Formanek, G. Schenz, W. Popp, H. Gatol, H. Zwick

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ABSTRACT: An incremental cycle ergometer test performed with a total of 40 healthy subjects (25 male, 15 female) was used to study the mechanical load on the ventilatory muscles. The parameters for the mechanical load on the ventilatory muscles are the time integral of the oesophageal pressure and the mean oesophageal pressure change per time unit ($dPoe/dTi$) of each breathing manoeuvre. The pressure-time integral is the area delimited by the oesophageal pressure trace and the inspiratory time axis. It is expressed as a fraction of the product of the subject's maximum oesophageal pressure (Poe_{max}) and total breath cycle duration (T_{TOT}). This parameter is called oesophageal tension time index (TTI_{oe}).

The relationship between minute ventilation and these two parameters during ergometer test showed gender-specific variations because of the differences between men and women as to anthropometric data, lung function parameters and maximum ventilatory muscle strength. Moreover, the $dPoe/dTi$ values significantly depend on the breathing frequency.

The present study has provided evidence that, in general, the TTI_{oe} and $dPoe/dTi$ values in terms of a specific minute ventilation (\dot{V}_E) are higher in women than in men. Parameters for the mechanical load on the ventilatory muscles regarding the level of pressure to be generated as well as the duration and velocity of muscle contraction should therefore also allow for the gender of the patients.

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In patients suffering from chronic obstructive pulmonary disease [1, 2] the ventilatory muscles play an important part in the limitation of physical exercise. There are several approaches to improve inspiratory muscle function such as pharmacological intervention [3], training modalities [4] or rest [5]. Proper assessment of the various therapeutic approaches requires information about the actual mechanical load on the ventilatory muscles in this group of patients. If possible, the parameters that serve as reference values for the mechanical load on the ventilatory muscles should allow for all factors that account for the energy consumption of the ventilatory muscles: 1) the tension developed; 2) the velocity of contraction; and 3) the duration of contraction [6].

For this purpose the oesophageal tension time index (TTI_{oe}) and the mean change of oesophageal pressure as a function of time ($dPoe/dTi$) was calculated from the data obtained at rest and through an incremental cycle ergometer test from 40 test persons (25 male, 15 female) without cardiopulmonary history. The TTI_{oe} reflects the mechanical load on the ventilatory muscles

as to the tension they have to develop and the duration of contraction. The $dPoe/dTi$ values reflect the velocity of muscle contraction. The correlation between minute ventilation (\dot{V}_E) and these two parameters was analysed.

Methods

Subjects and protocol

The study population was 40 volunteers, 25 male and 15 female subjects aged 14-50 yrs (mean age 27.1 yrs), all of whom were in a good physical condition. None of the subjects had any respiratory symptoms, nor did they show any sign of neuromuscular disease. Persons who had been smoking more than five cigarettes a day for the past five years were excluded. The anthropometric data and lung function data of the participants are given in table 1. All lung function parameters established were normal according to the reference values reported

by FORCHE [7]. Lung function tests, sniff trials and ergometric tests were performed on the same day, the sniff trials right before the exercise test. All tests were scheduled for the afternoon and all subjects had had lunch as usual at least two hours before the tests started. They were requested to abstain from drinking coffee or tea and smoking cigarettes.

Table 1. – Anthropometric and lung function data

		Males (n=25)	Females (n=15)
Age	yrs	30±11	22±9
Height	cm	183±8	169±7
Weight	kg	79±9	60±7
VC	l	6.21±0.93	3.93±0.46
VC	%pred	109±16	103±10
FEV ₁	l	4.92±0.86	3.25±0.39
FEV ₁	%pred	103±15	97±9
FEV ₁ %VC	%	79±6	82±7
TLC	l	8.97±1.22	6.11±0.66
TLC	%pred	119±18	105±8
RV	l	2.78±0.56	2.19±0.35
RV%TLC	%	31±4.7	36±3.5
Poe _{max}	cmH ₂ O	106±32	80±20
MVV	l·min ⁻¹	199±34	115±18

VC: vital capacity; FEV₁ forced expiratory volume in one second; TLC: total lung capacity; RV: residual volume; Poe_{max}: sniff-assessed maximal oesophageal pressure (1 cmH₂O=0.0981 kPa); MVV: maximal voluntary ventilation measured over 12 s; SD: standard deviation. Mean±SD.

Evaluation of respiratory muscle parameters

The oesophageal pressure at maximum sniff trials (Poe_{max}) was determined as a parameter for global respiratory muscle strength. It was measured by means of a flexible distilled water-perfused catheter (internal diameter 1.4 mm) inserted transnasally with the distal end of the catheter being placed in the middle third of the oesophagus. The catheter was first passed into the stomach with its distal end and, under observation of

the pressure signal, it was then withdrawn until it reached the middle third of the oesophagus [8]. The distance between the anterior nares and the distal end of the catheter was 35–40 cm on average. Two lateral foramina (diameter 1.8 mm) at the distal end of the catheter provided free communication with the surrounding area. The catheter was perfused with distilled water flowing at a constant rate of 25 ml·h⁻¹. The proximal end was connected to a pressure transducer (Gould-Statham, P23 ID). The pressure was displayed on a four channel strip-chart recorder (Beckman 511A), which showed the selected maximum amplitude to be reduced by 50% at 45 Hz.

The response time of the catheter-recorder system was examined by placing two bar-shaped electrodes into a sealed vessel made of polyethylene, containing 1 l of physiological saline solution (the remaining air space was about 2 cm³). The distal end of the water-perfused catheter was then positioned between the two electrodes (3 mm beside the imaginary connecting line). A current impulse of 80 Ws (I_{max} 40 A) caused an increase in pressure that was readily recordable. The 10–90% rise time (Tr) was found to be 0.02 s. The maximal frequency response (*f* 3 db) was determined from the equation *f* 3 db~1/3 Tr for the critically damped signal and was 17 Hz.

Sniffs were carried out at resting end-expiration (functional residual capacity (FRC)) and the oesophageal pressure was arbitrarily considered zero at the start of each sniff trial, therefore only pressure changes relative to the initial position were recorded. The volunteers were instructed that their sniffs be short, full strength and executed through the nose with the mouth closed. No use was made of noseclips. The period allowed between sniffs was 30–45 s. When a plateau of sniff Poe was reached (usually within 5 sniffs), an extra 10 maximum sniffs were carried out to make sure that there would be no further increase. The highest oesophageal pressure was then selected for analysis.

The time integral of the oesophageal pressure was calculated by plotting the relative oesophageal pressure changes against the time of each breathing manoeuvre

Table 2. – Breathing pattern and respiratory muscle parameters at maximal power output

		Males (n=25)	Females (n=15)	Significance of diff.
\dot{V}_E	l·min ⁻¹	141±24	86±13	p<0.001
fb	breaths·min ⁻¹	46±10	44±7	p>0.05
V _T	l	3.04±0.54	1.96±0.18	p<0.001
V _T /T _i	l·s ⁻¹	5.74±1.26	3.39±0.63	p<0.001
Power output	W	296±41	204±24	p<0.001
Poe	cmH ₂ O	46±11	41±11	p>0.05
dPoe/dT _i	cmH ₂ O·s ⁻¹	86±42	72±23	p>0.05
TTIoe		0.11±0.036	0.14±0.043	p<0.05

\dot{V}_E : minute ventilation; fb: frequency of breathing; V_T: tidal volume; V_T/T_i: inspiratory flow rate; Poe: oesophageal pressure; dPoe/dT_i: rate of change of Poe with respect to time (1 cmH₂O=0.0981 kPa); TTIoe: oesophageal tension time index; SD: standard deviation. Mean±SD.

at rest and while cycling and the end-expiratory pressure values of each breath were arbitrarily considered zero. For the recording of both the pressure-time curves and the sniff trials the same equipment was used.

Of the pressure-time graphs thus obtained, at least 8 breathing cycles of each load increment were chosen (2 breathing cycles per 30 s) the curves of which were completely free from artifacts (distortions of the curves caused by pressure changes because of oesophageal muscle contraction). These curves were blown up by photo-mechanical means and manually digitized (Numonics, 2210-0.30.c). The oesophageal pressure-time integral was calculated for each area delimited by the oesophageal pressure trace and the inspiratory time axis. It was expressed as a fraction of the product of the subject's maximum oesophageal pressure and total breath cycle duration (T_{TOT}). This parameter was called the oesophageal tension time index:

$$TTI_{oe} = \int_0^{T_i} P_{oe} dt / P_{oe_{max}} \times T_{TOT}$$

The pressure-time curves were also used to compute the mean change of oesophageal pressure as a function of time, which serves as a parameter for muscle contraction velocity.

Lung function and cycle ergometer testing

The volunteers' lung volumes were determined by means of a constant-volume whole body plethysmograph (Jaeger, Würzburg). The test exercises were performed in an upright sitting position on a cycle ergometer (Jaeger, Würzburg). The volunteers were allowed to rest for 2–4 min after the test devices had been connected. This period was long enough to reduce to a minimum the artifacts of the pressure-time curves caused by swallowing.

The resting period was followed by unloaded cycling for 4 min. The values obtained in this period were used as rest reference values. Starting from 25 W, the workload was then gradually increased by 25 W at two minute intervals up to a level of complete exhaustion. During the test the subjects were requested to keep their upright position in order to avoid pressure fluctuations because of changes in the body position.

Minute ventilation, tidal volume (V_T) breathing frequency (f_b) and oxygen uptake ($\dot{V}O_2$) were recorded every 30 s (Ergo Pneumotest, Jaeger, Würzburg). The respiratory flow was continuously recorded by means of the Beckman strip-chart recorder right below the oesophageal pressure tracing. The subsequent computation of inspiratory time (T_i), respiratory cycle duration (T_{TOT}) and the resultant T_i/T_{TOT} ratio was based on the flow recordings.

Statistical methods

Correlations were established by means of linear and nonlinear regression analyses. The level of significance was set at 0.01 ($p \leq 0.01$). The data are presented as mean \pm standard deviation (sd).

Results

Breathing pattern and ventilatory muscle parameters during exercise

Breathing pattern and respiratory muscle parameters at maximal power output are given in table 2. Data reveal significant gender-specific differences in view of \dot{V}_E , V_T , V_T/T_i , TTI_{oe} and power output, while there were no significant differences as to f_b , P_{oe} and

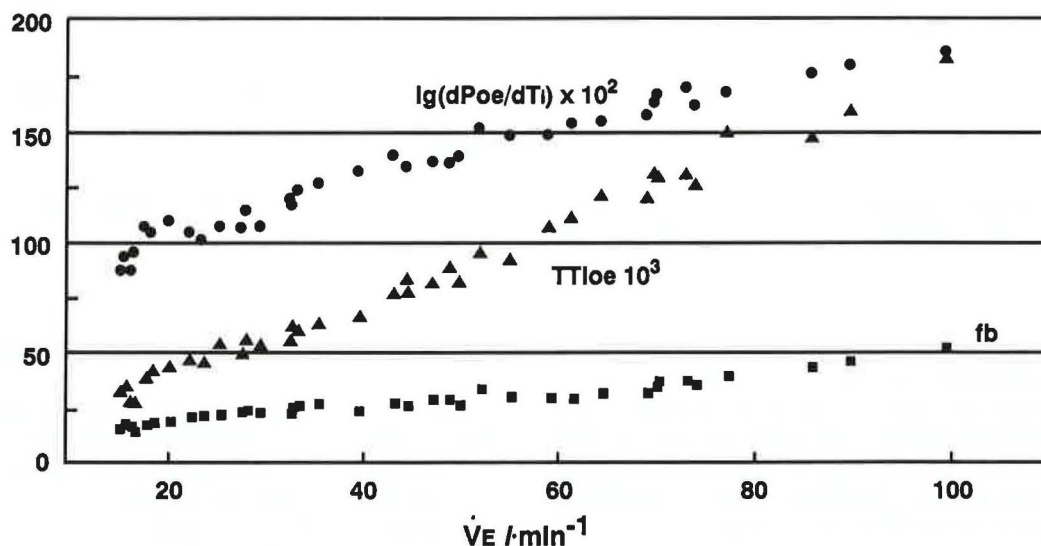


Fig. 1. — Representative plot of one female subject during ergospirometry. Breathing frequency (f_b), the oesophageal tension time index (TTI_{oe}) and the logarithmic rate of change of oesophageal pressure with respect to time ($\lg(dP_{oe}/dT_i)$) are plotted versus minute ventilation (\dot{V}_E).

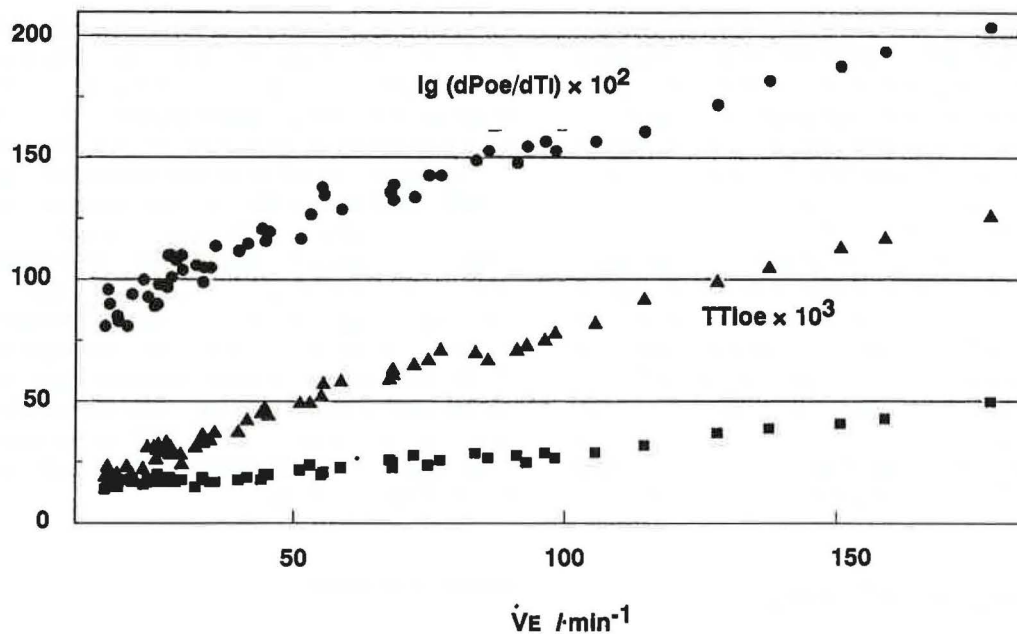


Fig. 2. - Representative plot of one male subject during ergospirometry. For abbreviations see legend to figure 1.

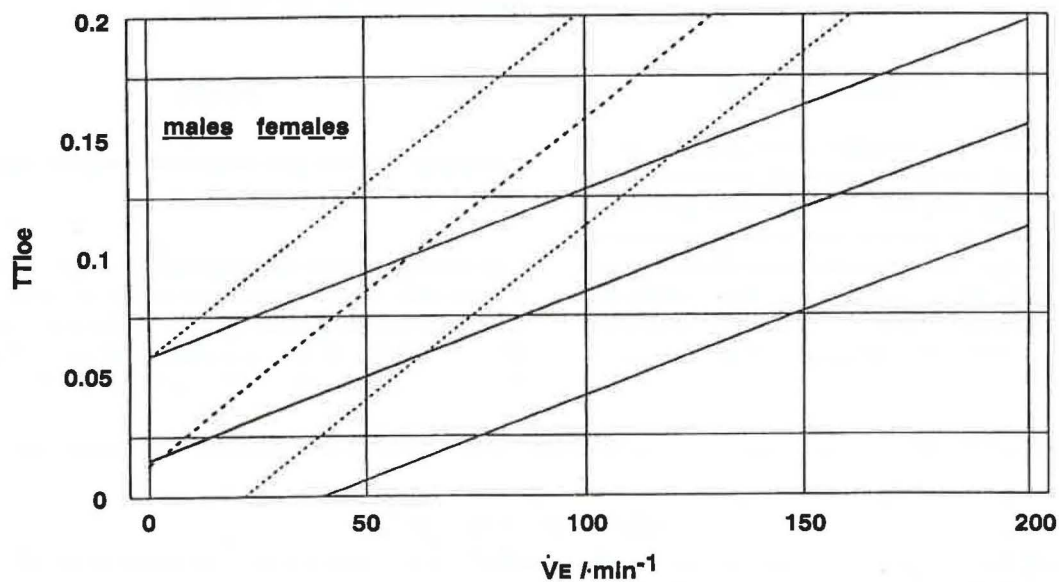


Fig. 3. - Relationship between minute ventilation (\dot{V}_E) and oesophageal tension time index (TTIoe) during cycle ergometer test. Regression line and confidence interval (95%) for male (—) and female subjects (---).

$dPoe/dTi$. At maximum workload all test subjects had a respiratory exchange ratio (R) of more than 1.05.

In all test persons, the increase in ventilation at low levels of work was mainly due to the increase in tidal volume. The curve representing the relationship between V_T and \dot{V}_E was largely hyperbolic, with V_T increasing to an asymptote at 50–60% of the vital capacity. For both gender groups an individual representative plot of f_b , TTIoe, and $g(dPoe/dTi)$ against \dot{V}_E is given in figure 1 and figure 2.

The TTIoe- \dot{V}_E and $dPoe/dTi$ - \dot{V}_E relationship

Cluster analysis enabled us to divide the measured data for the TTIoe- \dot{V}_E relationship and the $dPoe/dTi$ - \dot{V}_E relationship into two homogeneous groups, which largely corresponded to the measuring data broken down according to gender. The mean values computed for the two groups were practically identical with the mean values of our female and male subjects. From then on men and women were analysed separately.

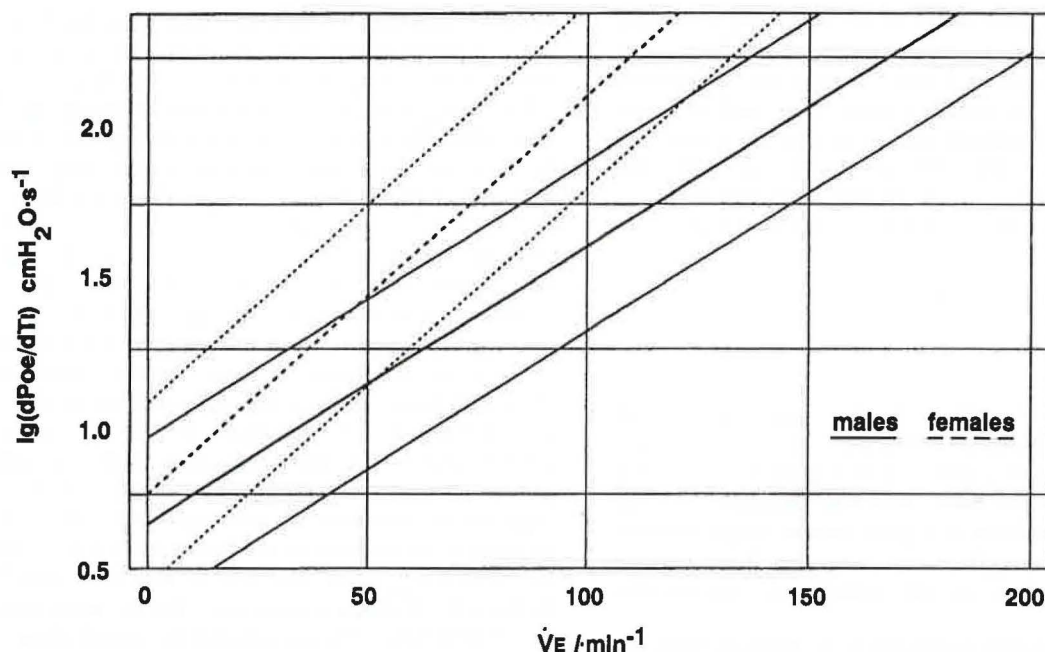


Fig. 4. — Relationship between minute ventilation (\dot{V}_E) and the logarithmic rate of change of oesophageal pressure with respect to time $\lg(dPoe/dTi)$. Regression line and confidence interval (95%) for male (—) and female subjects (---).

It was demonstrated that there was a linear correlation between \dot{V}_E and $TTIoe$ in both men and women (fig. 3).

The correlation for women was:

$$TTIoe = 0.0014438 \times \dot{V}_E + 0.0134 \quad (n=15, r=0.84, p<0.01)$$

The correlation for men was:

$$TTIoe = 0.0006968 \times \dot{V}_E + 0.01534 \quad (n=25, r=0.70, p<0.01)$$

$TTIoe$ at maximal workload for women was 0.14 ± 0.043 , and for men 0.114 ± 0.036 . Correlation between \dot{V}_E and $dPoe/dTi$ was of an exponential type (fig. 4).

For female subjects:

$$\lg(dPoe/dTi) = 0.01370 \times \dot{V}_E + 0.7510 \quad (n=15, r=0.88, p<0.01)$$

For male subjects:

$$\lg(dPoe/dTi) = 0.00955 \times \dot{V}_E + 0.6509 \quad (n=25, r=0.91, p<0.01)$$

$dPoe/dTi$ at maximal workload for women was 71.5 ± 22.5 , and for men 86.4 ± 41.8 $\text{cmH}_2\text{O} \cdot \text{s}^{-1}$.

Correlations between the ventilatory muscle parameters and exercise measured parameters

There was no evidence of any correlation between V_T , f_b , V_T/Ti on the one hand and $TTIoe$ (and hence the $TTIoe$ - \dot{V}_E relationship) on the other. The $dPoe/dTi$ however, was correlated with f_b , with no significant difference between the two gender groups. For the overall sample we found the relationship:

$$\lg(dPoe/dTi) = 0.034 \times f_b + 0.402 \quad (r=0.83, n=40, p<0.01)$$

Table 3. — Correlations of the slopes (K_1 , K_2) and anthropometric and lung function data

		$r(K_1)$	$r(K_2)$
Height	cm	-0.63	-0.60
Weight	kg	-0.64	-0.68
VC	l	-0.62	-0.59
FEV ₁	l	-0.62	-0.55
TLC	l	-0.62	-0.62
R_{total}	$\text{kPa} \cdot \text{l}^{-1} \cdot \text{s}^{-1}$	0.53	0.36
Poe_{max}	cmH_2O	-0.59	-0.43
MVV	$\text{l} \cdot \text{min}^{-1}$	-0.63	-0.50

1 $\text{cmH}_2\text{O} = 0.0981$ kPa. K_1 : $TTIoe/\dot{V}_E$; K_2 : $\lg(dPoe/dTi)/\dot{V}_E$. VC: vital capacity; FEV₁: forced expiratory volume in one second; TLC: total lung capacity; R_{total} : airway resistance; Poe_{max} : sniff-assessed maximal oesophageal pressure; MVV: maximal voluntary ventilation measured over 12 s.

Since the f_b of all women was invariably higher on every level of minute ventilation, the pertaining $dPoe/dTi$ -values were also higher. Apart from physical characteristics and lung function parameters, the $dPoe/dTi$ - \dot{V}_E relationship was therefore influenced by the subjects breathing pattern.

Ventilatory muscle parameters, physical characteristics and lung function parameters

To find a correlation between the measured ventilatory muscle parameters on the one hand and physical characteristics or lung function parameters on the other, we computed the slopes for the regressions of

TTIoe on \dot{V}_E (K_1) and of $dPoe/dT_i$ on \dot{V}_E (K_2) for each subject. K -values were examined for linear and non-linear correlations. Table 3 shows the correlation coefficients for the entire sample. The multiplicative model produced significant correlations, where the best correlation coefficient (r) found was 0.68. All parameters examined were inversely related to K_1 or K_2 . Only total airway resistance showed a positive relationship.

Quality control

In order to verify intra-individual reproducibility of the measured parameters, 15 men and 8 women performed another sniff trial and cycle ergometer test within two weeks. In accordance with the literature [9], the ergospirometric indices at a given power output showed no major intra-individual variations. For \dot{V}_E at a given \dot{V}_E we could not prove any significant between-day variation.

The intra-individual variations were deduced from the coefficient of variation (CV). On each load increment, both for TTIoe and $dPoe/dT_i$ 8 test values were recorded per day. The intra-individual variation of the oesophageal tension time index ranged from 5.5–9.4% (mean 7.3%). For $dPoe/dT_i$ the CV ranged from 3.8–7.8% (mean 5.9%). Reproducibility was also excellent for the values of maximum inspiratory muscle strength. Between the two days of testing the values of Poe_{max} varied by an average of 5.2 cmH₂O (range 2.0–6.2 cmH₂O).

Discussion

The aim of this study was to examine the load on the ventilatory muscles during exercise in healthy subjects. The parameters used were chosen because they were to reflect the energy consumption of the ventilatory muscles. The energy consumption of skeletal muscle contraction depends on the tension developed, the duration of contraction and the velocity of muscle shortening [6].

The mechanical work of breathing as estimated by both AGOSTINI *et al.* [10] and GOLDMAN *et al.* [11] does not allow for the duration of contraction. Therefore, breaths with equal tidal volume but different inspiratory time may have the same pressure-volume relationship, thus performing the same amount of work; longer breaths, however, are more energy-consuming.

Recent investigations have introduced the so-called pressure-time integral, a new parameter for the calculation of the ventilatory muscle load. In these studies, the pressure was taken in the mouth or in the oesophagus or it was given as transdiaphragmatic pressure [12–15]. The integral allows for the duration of contraction and the tension of the respiratory muscles they have to develop, and so it perfectly reflects the oxygen consumption of the ventilatory muscles. The amount of

energy consumed by skeletal muscle contraction obviously depends on the initial state of contraction as well, which is not being allowed for in the TTIoe.

The Poe_{max} values used in the calculation of the TTIoe were obtained at functional residual capacity at rest. In healthy subjects the end-expiratory lung volume decreases with physical exercise. The inspiratory muscle capacity to generate pressure improves with decreasing intrathoracic gas volume [16], so that the Poe/Poe_{max} ratio obtained from measurements under load is actually a little lower. Accordingly, the TTIoe obtained under load is slightly lower than that found in our study.

Since the relaxation pressure-volume curves of the chest wall were not recorded, the exact proportion of the pressures which had been exerted by active muscle contraction and which were measured in the oesophagus, cannot be definitely stated. Yet, it remains clear that vigorous recruitment of the inspiratory muscles was necessary. At maximum workload the ratios of inspiratory Poe/Poe_{max} were $48 \pm 14\%$ in men and $54 \pm 15\%$ in women. Even taking into account that the ratios may have been a little lower, these pressures presented a heavy load on the inspiratory muscles. By measuring the transdiaphragmatic pressure of healthy subjects, another study provided evidence that diaphragmatic fatigue occurred when the transdiaphragmatic pressure to be generated exceeded 40% of the maximum transdiaphragmatic pressure [17].

In our study we measured the oesophageal instead of the transdiaphragmatic pressure, since the gastric proportion of the transdiaphragmatic pressure is inversely proportional to the workload [18]. This is largely due to the fact that recruitment of the intercostal accessory muscles steadily increases with increasing workload, which would have to be taken into account when transdiaphragmatic pressures are measured under load.

Certainly, the decrease of the gastric pressures during inspiration under load may also be due to the fact that the increasing load causes the abdominal muscles to contract more strongly during expiration and to relax more and more during the following inspiration. This behaviour of the abdominal muscles results in optimum diaphragm length and consequently, lowers active force generation required by the diaphragm for inspiration.

The amount of energy consumed by the ventilatory muscles depends on the contraction velocity as well [6]; so the mean change of oesophageal pressure as a function of time appears to be a useful parameter. In many cases the rate of inspiratory flow was used as an indirect parameter for the rate of inspiratory muscle shortening (and, consequently, for the muscle contraction velocity) [14]. However, recent studies employing sonomicrometry in animal experiments (dogs), failed to establish a causal relationship between inspiratory air flow and the shortening velocity of the diaphragmatic muscle [19, 20]. That is why we used the $dPoe/dT_i$ as a parameter for muscle contraction velocity.

The study demonstrated that both the TTIoe- \dot{V}_E and the $dPoe/dT_i$ - \dot{V}_E relationship are influenced by physical characteristics, lung function parameters and maximum pressure values yielded by the sniff trial.

Certainly, each subject's inspiratory system impedance was influenced by the individual physical characteristics. Since the male subjects were invariably taller than the female subjects, they had larger lungs and higher respiratory volumes. Therefore, the lungs of the male volunteers were more compliant and the airway resistance was lower.

What is more, the maximum global inspiratory muscle strength (Poe_{max}) was higher in men. It is the above differences between men and women that support the findings of the present study according to which women, in relation to a given minute ventilation, invariably showed higher TTI_{oe} .

We could not prove any correlation between the subject's breathing pattern and the TTI_{oe} . This is due to the fact that the size of the area delimited by the oesophageal pressure trace and the inspiratory time axis (the oesophageal pressure-time integral) did not correlate with the breathing frequency or tidal volume. An area of the same size may also result from high pressure and short inspiratory time, or from low pressure and long inspiratory time, respectively. The Poe_{max} is by no means influenced by the breathing pattern either and it is these two factors, that is, the oesophageal pressure-time integral and the Poe_{max} , that have the main impact on the TTI_{oe} .

On the contrary, at least the $dPoe/dTi \cdot \dot{V}_E$ relationship was clearly affected by the subject's breathing pattern: the higher the breathing frequency, the higher the $dPoe/dTi$ values. The female subjects showed higher breathing frequencies at a given \dot{V}_E and therefore steeper slopes of the $dPoe/dTi \cdot \dot{V}_E$ regression.

Owing to the significant differences between men and women with regard to physical characteristics, lung function parameters, maximum oesophageal pressure yielded by the sniff trial, and breathing pattern at each minute ventilation, we found ventilatory muscle load to be constantly higher in the female group.

If gender-related reference values are used, it is possible to determine the degree of increase of the ventilatory muscle load in patients suffering from chronic obstructive pulmonary disease by comparing the values recorded at a specific minute ventilation. Only exact determination of the degree of load increase in this group of patients will prepare the ground for further studies evaluating the effectiveness of the various therapeutic approaches with regard to the improvement of ventilatory muscle function. In the literature their respective values are still debated by the medical profession.

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Charge mécanique sur les muscles ventilatoires pendant un test progressif à la bicyclette ergométrique chez des sujets sains, hommes et femmes. T. Wanke, D. Formanek, G. Schenz, W. Popp, H. Gatol, H. Zwick.

RÉSUMÉ: La charge mécanique sur les muscles ventilatoires a été étudiée par un test progressif à la bicyclette ergométrique réalisé sur un total de 40 sujets sains (25 hommes et 15 femmes). Les paramètres pour apprécier la charge mécanique des muscles ventilatoires sont l'intégrale de temps de la pression oesophagienne et les modifications moyennes de pression oesophagienne par unité de temps (dP_{oe}/dT_i) lors de chaque manœuvre respiratoire. L'intégrale pression-temps est la surface délimitée par le tracé de pression oesophagienne et l'axe du temps inspiratoire. Elle est exprimée comme une fraction du produit de la pression oesophagienne maximale du sujet (P_{oemax}) et la durée totale du cycle respiratoire (T_{TOT}). Ce paramètre est appelé l'index de temps de tension oesophagienne (TTI_{oe}). La relation entre la ventilation minute et ces deux paramètres au cours d'une

test ergométrique a montré des variations liées au sexe, en raison des différences entre hommes et femmes pour ce qui concerne les données anthropométriques, les paramètres fonctionnels pulmonaires, et la force musculaire ventilatoire maximal. De plus, les valeurs de dP_{oe}/dT_i dépendent significativement de la fréquence ventilatoire. L'étude actuelle a montré, qu'en général, les valeurs de TTI_{oe} et de dP_{oe}/dT_i en terme de ventilation minute spécifique (\dot{V}_E) sont plus élevées chez les femmes que chez les hommes. Les paramètres pour la charge mécanique des muscles ventilatoires, en ce que concerne le niveau de pression à générer, ainsi que pour la durée et la vélocité de la contraction musculaire, devraient donc prendre en compte également le sexe des patients.

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